

## **RECOMBINANT BACTERIAL VACCINE SYSTEM WITH ENVIRONMENTALLY LIMITED VIABILITY**

### **Abstract of the Invention**

Disclosed is an Environmentally Limited Viability System (ELVS) for microorganisms based on temperature differences between permissive and non-permissive environments. Viability of the microorganisms are limited to the permissive environment by specifically expressing one or more essential genes only in the permissive environment, or expressing one or more lethal genes only in the non-permissive environment. Environmentally Limited Viability Systems are also disclosed involving coordinate expression of a combination of required genes and lethal genes. Microorganisms containing an Environmentally Limited Viability System are useful for release into a permissive environment. Temperature regulated Environmentally Limited Viability Systems are particularly suited for use with recombinant avirulent *Salmonella* vaccines by limiting their growth to the warmer environment inside the host. Such vaccines can be administered to protect humans or warm-blooded animals against bacterial, viral, mycotic and parasitic pathogens, especially those that colonize on or invade through mucosal surfaces. This antigen delivery system can also be used for expression of gamete-specific antigens to induce immune responses to block fertilization, or to induce immune responses to tumor antigens. In the event that an individual sheds live vaccine into the environment, the presence of the ELVS prevents survival of the vaccine. When environmentally regulated lethal genes are present on an extrachromosomal element and are regulated by chromosomal genes, transfer of the extrachromosomal element to other microorganisms will be limited by unregulated expression of the lethal genes in the recipient microorganism.

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